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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/706,801	11/12/2003	Francine M. Foss	00398-152001 / NEMC 263;	6989

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EXAMINER	
HAMUD, FOZIA M	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/706,801	FOSS ET AL.	
	Examiner	Art Unit	
	Fozia M. Hamud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-7,9-11 and 31-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-7, 9-11, 31-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Response to Amendment

1a. Receipt of Applicants' amendment and arguments, filed on 17 July 2006 is acknowledged.

Status of Claims:

1b. Claims 2, 8, 12-30 have been cancelled, new claims 34-36 have been added. Thus, claims 11, 3-7, 9-11 and 31-36 are pending and under consideration.

1c. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. The following previous objections and rejections are withdrawn in light of Applicants' amendment filed 07/17/06.

(I) All of the rejections made against cancelled claims 2 and 8 are moot.

(II) The rejection of claims 1-11 and 31-33 made under 35 U.S.C. 112, second paragraph, is withdrawn, because the indefinite limitations have been deleted.

(III) The rejection of claims 1, 7-11 and 31 made under 35 U.S.C §102(a) as being anticipated by VanderSpeck et al (March 2002) as well as the rejection of claims 1 and 32-33 made under 35 U.S.C. 103(a) as being unpatentable over VanderSpeck et al in view of Capon et al., U.S. Patent Number 5,116,964, are withdrawn, because of the Declaration filed under 37 CFR 1.131, by Applicant Foss is found persuasive.

(IV) Claim 1 made under 35 U.S.C. 102(b) Gregoire et al (October 2001), withdrawn, because amended claim 1 does not encompass the anticipated limitations.

New Rejections Necessitated by Applicants' Amendment:

Claim Rejections under 35 U.S.C. §112, First paragraph:

3a. Claims 1, 3-7, 9-11, 31-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide comprising the polypeptide of SEQ ID NO:1, wherein there is a mutation at the position corresponding to position 143 of said SEQ ID NO:1, said mutant which binds to IL-7R, does not reasonably provide enablement for non-human IL-7 amino acid sequences that have a mutation at the position corresponding to position 143 of SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make or use the invention commensurate in scope with these claims.

Claims 1, 3-5 encompass "....non-human IL-7 amino acid sequences that have mutations at the position corresponding to position 143 of SEQ ID NO:1", However, the instant specification discloses only IL-7 mutants where there is substitutions at position 143, for example, where tryptophan at position 143 of the mature IL-7, (position 167 of the full length IL-7) is substituted with alanine, histidine, tyrosine or praline, (see page 20, lines 21-28). The specification fails to disclose a mutant of IL-7, in which an amino acid is added at position 143, or wherein an amino acid is deleted at position that retains the desired activity. The specification further discloses that said mutants bind to IL-7 receptor with less affinity compared to native IL-7 and induce proliferation of IL-7 dependent 2E8 cells, (see page 18, lines 26-30). The instant specification does not disclose any non-human IL-7 amino acid sequences that have mutation at the position corresponding to position 143 of SEQ ID NO:1. For example, the murine IL-7 amino acid sequence consists of 154 amino acid residues, while the human IL-7 consists of

177 amino acid residues. The human IL-7 contains a Tryptophan at position 167 of the full length, which corresponds to position 143 of the mature human IL-7, however, since the murine IL-7 only consists of 154 amino acids, there is no position that corresponds to position 167 of the human IL-7. Furthermore, Applicants have not shown that mutating a non-human IL-7 at position that corresponds to position 143 of SEQ ID NO:1, that results in a mutant that binds IL-7 receptor. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of which non human IL-7 polypeptides would tolerate a mutation at an amino acid residue that corresponds to 143 of SEQ ID NO:1, would tolerate deletion or addition and would still retain the desired activity. It is this additional characterization of the disclosed protein that is required in order to obtain the functional and structural data needed to permit one to produce a polypeptide which meets both the structural and functional requirements of the instant claim that constitutes undue experimentation. Regarding claims 3, 4 the specification does disclose an IL-7 mutant where there is an addition or a deletion at position 143 of SEQ ID NO:1, that retains the desired activity.

The criteria set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those

in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, is the basis for determining undue extermination. In the instant case, Due to the large quantity of experimentation necessary to generate the infinite number of IL-7 mutants recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which residues tolerate alterations, where to add additional amino acid residues, in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections under 35 U.S.C. §112, second paragraph:

4. Claims 1, 3-7, 9-11, 31-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

4a. Claims 1, 3, 4, 5, recite "....non-human IL-7 amino acid sequence that has a mutation at the position corresponding to position 143 of SEQ ID NO:1", however, this renders these claims indefinite, because it is unclear which "....non-human IL-7 amino acid sequence" is being referred to? Furthermore, not all non-human IL-7 amino acid sequences contain an amino acid that corresponds to "position 143". For example, the murine IL-7 amino acid sequence consists of 154 amino acid residues, while the human IL-7 consists of 177 amino acid residues. The human IL-7 contains Tryptophan at

position 167 of the full length, which corresponds to position 143 of the mature human IL-7, however, since the murine IL-7 only consists of 154 amino acids, there is no position that corresponds to position 167 of the human IL-7. Appropriate correction is required.

4b. Claims 3, 4 recite "....wherein the mutation comprises an addition of an amino acid at position 143 of SEQ ID NO:1", however, this renders these claims indefinite, because it is unclear whether the amino acid is added before or after position 143.

Claims 6-11 and 31-36 are vague and indefinite so far as they depend from claim 1 for the limitations set forth directly above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5a. Claims 1, 5-7, 9, 31, 34-35 and 36 are rejected under 35 U.S.C. 102(b) Cosenza et al (May 2000).

The instant claims 1, 5-7, 9, 31, 34-35 and 36 are drawn to IL-7 mutant polypeptides, wherein there is a mutation at the position corresponding to position 143 of SEQ ID NO:1, said mutant which effectively competes with wild type IL-7 for binding.

Cosenza et al disclose several IL-7 mutants. One of the mutants disclosed in the Cosenza et al reference, the tryptophan residue at position 143 of wild type human IL-7 is replaced with alanine (W143A), (see page 916, figure 7 and table 2 on page 923).

The authors studied the binding affinity of the IL-7 mutants and its ability to stimulate 2E8 cell proliferation. They demonstrated that the W143A mutant binds to IL-7R with much higher EC50 than wild type and that it abrogates 2E8 cell proliferation, (see figures 7, page 924, column 1 and table 2).

Therefore, the Cosenza et al reference meets all the limitations recited in instant claims 1, 5-7, 9, 31, 35 and 36, thus anticipating theses claims in the absence of any evidence on the contrary.

Claim Rejections under 35 U.S.C. §103:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6a. Claims 1 and 10, 32-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cosenza et al in view of Capon et al., U.S. Patent Number 5,116,964.

The instant claims 10 and 31-33 are drawn to a mutant of IL-7, wherein the tryptophan at position 143 is replaced with a histidine or a tyrosine, and said mutant further fused to a heterologous polypeptide, which increases the half life of the IL-7 polypeptide.

The teachings of Cosenza et al are discussed directly above. However, Cosenza et al does not teach a mutant in which the tryptophan at position 143 is replaced with a histidine or a tyrosine or a chimera of IL-7 mutant.

With respect to claim 10, Cosenza et al teach a method of producing IL-7 mutants and a way of testing their binding capacities and effect of cell proliferation. Therefore, one skilled in the art could easily have follwed the teachings of Cosenza et al and produce a mutant in which trypophan at position 143 was replaced with either a histidine or tyrosine.

With respect to claims 32-33, Capon teaches fusion proteins comprising immunoglobulin polypeptide fused to "ligand binding partners", which are defined as including hormones and growth factors (see column 2, lines 14-19). At column 4, lines 38-43, Capon states that the immunoglobulin (Ig) fusions of the invention "serve to prolong the in vivo plasma half-life of the ligand binding partner..." and "facilitate its purification by protein A". Also taught are recombinant materials for making such a fusion protein, vectors and expression; see columns 15-16. Preferred embodiments include sequences including the hinge regions of IgG-1, -2, -3 or -4, IgA, IgE, IgD and IgM, see column 14, lines 40-45 (the first domain of the constant region can be omitted). The preferred species of Ig was human, (see claims 8-9). Capon states that the DNA sequences for the Ig chains were well known in the art at the time the invention was made, see column 15 beginning at line 40.

Therefore, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the polypeptide of Cosenza et al et al to make fusion proteins as taught by Capon et al. The person of ordinary skill in the art would have been motivated to make the modification in view of Capon's disclosure that fusion proteins facilitate purification of desired proteins and prolong the in vivo half life.

Accordingly, the invention, taken as a whole, is prima facie obvious over the cited prior art.

Conclusion:

8. No claim is allowed. Claims 3, 5 and 20, would be allowable if rewritten to overcome the rejection under 35 U.S.C. 112, first paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information:

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia M. Hamud whose telephone number is (571) 272-0884. The examiner can normally be reached on Monday-Thursday, 6:00 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda G. Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Patent Examiner
Art Unit 1647
01 October 2006

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